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INCREASING SURVIVAL AND PREVENTION OF MYOCARDIAL INJURY IN RATS SUBJECTED TO CHRONIC ETHANOL ADMINISTRATION WITH FRUCTOSE 1-6 DIPHOSPHATE (FDP).

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Chronic ethanol administration to animals causes not only decrease in oxidative phosphorylation in the myocardium but also diminishes catabolic activity of glycolysis and as a consequence can produce tissue injury. Fructose 1-6 diphosphate (FDP) has been shown to restore activity of glycolysis in ischemic and hypoxic states. In view of that we investigated whether FDP will protect the myocardium against ethanol toxicity. Rats (#43) whose ethanol intake (orally and parenterally) was 30% of their daily caloric requirements were treated daily with FDP (#16) and those serving as controls with glucose (#8) or 0.9% NaCl (#8). Thirteen rats (#13) rats were not treated but received the same amount of ethanol. The rats surviving 4 weeks were killed and biopsies were obtained for light and electron microscopy studies. Survival in the FDP group was 75% whereas for all controls was 35% ($p<0.02$). There was no difference in mortality among the control subgroups. Light microscopy revealed in 50% of the controls myocardial damage whereas in the FDP specimens, no abnormalities were detected. In those controls that light microscopy revealed no detectible abnormality, electron microscopy showed in all of them subcellular injury. In contrast, electron microscopy in all the FDP treated rats revealed normal subcellular myocardial morphology. Despite that the rats received very high (toxic) ethanol doses, FDP administration decreased significantly mortality and protected the myocardium against the ethanol-induced injury.

INFLUENCE OF INTRAMYOCARDIAL BLOOD VOLUME IN THE QUANTITATION OF MYOCARDIAL PERFUSION USING EXTERNAL DENSITOMETRIC MEASUREMENTS

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Techniques employing external densitometric measurements of myocardial perfusion have been limited in their application because of underestimation of high flow rates. However, it is known that at high flow rates, intramyocardial blood volume (BV) increases. Thus, in-vivo densitometric measurements of flow (measured per unit volume) may not correlate with flow per unit mass when microspheres are used as a reference measurement. We examined the effect of accounting for BV on the correlation between in-vivo measurements of flow (using fast CT) and microspheres (M) in 8 closed chest, anesthetized dogs (18-24 kg) with myocardial flow rates of 52-371 ml/100 g/min. BV was determined as the ratio of the areas under the time density curves from the myocardium and the left ventricular cavity. The lateral wall of the left ventricle was used as the region of interest as this was associated with the least imaging artifacts. Fast CT estimates of BV varied from rest to maximum vasodilation (5-35%). Prior to accounting for BV, the correlation between CT measurements (ml/100 g/min) and flow by M was: 0.70 M + 40 ($r = 0.80$, SEE = 40). After accounting for BV, the accuracy improved to: 0.95 M + 24 ($r = 0.81$, SEE = 63).

We conclude that accounting for changes in BV improves the accuracy of high myocardial blood flow rates when using external densitometric measurements of myocardial perfusion.

Wednesday, March 21, 1990
8:30AM–10:00AM, Room 23
Cardiovascular Magnetic Resonance and Computed Tomography

RIGHT VENTRICULAR PERFORMANCE IN LUNG DISEASE

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To determine RV systolic performance in severe lung disease (SLD), we studied ten subjects free of cardiopulmonary disorders and 24 pts. with chronic (symptoms 6.3 ± 2 yrs.) SLD. Fifteen had obstructive and 9 interstitial SLD; all had resting PA hypertension (45 ±20)mm Hg and desaturation (p O^2 91±5)%. Rest and peak bicycle exercise contrast enhanced Cine Computed Tomograms (CT) and Doppler echocardiograms were obtained. A RV contractility index (P/V) was derived as the slope of the regression line relating peak PA systolic pressure (PASP) and normalized RV end systolic volume (ESV). Additionally, RV ejection fraction (EF), stroke volume (SV), and end diastolic (EDV) volumes also normalized for body size, were determined. Measurements were obtained in room air (RA) and with oxygen enrichment (40 % O^2).

	P/V*	PASP*	RVEF*	RVESV*	RVSV*	RVEDV*
Normal	.4 ±.1†	35 ±7†	57 ±3†	43 ±5	56 ±6	99±16†
Lung/ RA	.7 ±.3	78 ±5	46 ±2	44 ±3	38 ±2	110± 9
Lung/ O^2	.7 ±.2	71 ±5	45 ±2	44 ±3	37 ±2	136±12

* = at peak bicycle exercise, † = p is at least ≤ .05 (SLD vs normals)

The RV contractility index (P/V) is significantly higher in SLD than in normals. The disparity between the P/V and the decreased RV ejection fraction in SLD, is due to an increase in afterload (PASP), a lower exercise performance, and a decrease in stroke volume that is incompletely compensated by elevation of EDV. Conclusions: Cine CT combined with Doppler echocardiograms enhances analysis of RV function. The P/V demonstrates that RV systolic performance is enhanced in SLD. The well known lowered RVEF of SLD is a poor indicator of RV function because EF is dependent upon afterload and the vagaries of ventricular volume responses to exercise and hypoxia. Thus, the RV contractility index is more clinically useful than RVEF in evaluation of RV systolic performance in SLD.

QUANTITATIVE ASSESSMENT OF REDUCTIONS IN SUBENDOCARDIAL AND FULL-THICKNESS REGIONAL FLOW RESERVE DURING PROGRESSIVE CORONARY STENOSIS USING ULTRAFAST COMPUTED TOMOGRAPHY.

John M. Canty, Jr., M.D., F.A.C.C., Alan Brody, M.D. and Francis J. Klocke, M.D., F.A.C.C.. SUNY at Buffalo, N.Y.

Regional reductions in subendocardial and full-thickness flow reserve distal to a coronary stenosis have been assessed in closed-chest dogs using Ultrafast Computed Tomography (CT). Animals chronically instrumented with a left circumflex (LC) artery Doppler flow probe, hydraulic occluder and distal LC catheter were studied during maximum vasodilation (adenosine 5-10 mg/min i.v.). High resolution (.7 mm x .7 mm x 3 mm thick voxel) short-axis diastolic LV tomograms were obtained during 20 successive cardiac cycles at selected levels of distal LC pressure reduction. To circumvent beam hardening artifacts, non-ionic contrast was infused into the aortic root (3 ml/sec for 10 seconds). Vasodilated flow in the stenotic LC region (n=12) was compared to vasodilated flow in the normally perfused anterior region (LAD) by determining the change in myocardial CT number (minus background) during the aortic infusion (ΔCT), and the time to achieve 50 percent of this change (T_{50}) by the following equation: LC/LAD flow reserve ratio during vasodilation = $(\Delta CT/T_{50})_{LC}/(\Delta CT/T_{50})_{LAD}$. There was a nearly one to one relation between the CT derived full-thickness LC/LAD flow reserve ratio (y) and relative reductions in LC Doppler flow velocity (x): $y = 1.09 x - .10$, $r = 0.93$. Ultrafast CT derived reductions in subendocardial flow were also linearly related to reductions in Doppler flow velocity: $y = 0.94 x - .05$, $r = 0.90$. We conclude that high resolution Ultrafast Computed Tomography offers promise for defining the physiological significance of a wide range of coronary stenoses, including those with transstenotic pressure gradients as small as 10 mm Hg during maximum vasodilation. The evaluation of spatial differences in flow during vasodilation may minimize effects of factors which can confound traditional flow reserve measurements.